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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,798	11/02/2001	Camellia W. Adams	P1101R2D1	4012

9157 7590 10/02/2003

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	13

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,798	ADAMS ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-62 and 65-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-62,65-75,79-89 and 93-97* is/are rejected.

7)☒ Claim(s) *76-78 and 90-92* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

1. Claims 59-62 and 65-97 are pending in the instant application.

Election/Restrictions

2. Applicant's election of the species of monoclonal antibody 16E2 in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Drawings

3. The formal drawings filed April 17, 2002 are acceptable.

Priority Statement in First Line of Specification

4. This application filed under former 37 CFR 1.60 lacks the current status and the filing date of the nonprovisional parent application 09/079,029. See 37 CFR 1.78.

Sequence Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicant is given the statutory time from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

In particular, there are sequences in Figure 2B that are not present in the sequence listing. M.P.E.P. 2422.02 states: "It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO: X") must be used, either in the drawing or in the Brief Description of the Drawings."

Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences recited in the claims and specification of the instant application which are encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). **The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence.** For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Specification

6. The disclosure is objected to because of the following informalities:

6.1 37 C.F.R. §1.821(d) states:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Sequences are disclosed in Figures 2A and B and 16 without the required reference to the sequence identifiers. Also, the instant specification needs to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. This can

be resolved by adding a reference to the Figures or the Brief Description of the Drawings. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Applicants are required to amend the specification and claims to comply with 37 C.F.R. §1.821(d).

6.2 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Inducing apoptosis using anti-APO-2 antibodies.

Claim Objections

7. Claims 76-78 and 90-92 are objected to because of the following informalities: the 16E2, 20E6 and 24C4 antibodies should be referred to by their sequence identifiers in the claims. See section 6 above and 37 C.F.R. §1.821(d).

Appropriate correction is required.

Oath/Declaration

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specifically, the correction of the spelling of inventor Camellia W. Adams was not initialed or dated.

Formal Matters

9. The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see MPEP Chapter 2400 and 37 C.F.R."1.801-1.809). Examiner acknowledges the deposit of organisms under accession number ATCC HB-12456 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in compliance with this requirement (see specification, page 95).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 59-62 and 65-75, 79-89 and 93-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 10-47 of copending Application No. 09/396,746, and claim 14 of copending Application No. 10/207,295. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to a method of inducing apoptosis in mammalian cancer cells or treating mammalian cancer cells in vivo or ex vivo by exposing the cells to a monoclonal antibody that binds Apo-2 polypeptide of SEQ ID NO: 1 or binds the soluble extracellular

domain of amino acids 1- 182 or 54-182 of SEQ ID NO: 1, wherein the antibody comprises a single-chain antibody, is a chimeric antibody, a humanized or human antibody, comprises a Fab fragment, scFv or F(ab')2 fragment, fused to an epitope tag sequence, wherein the cancer cells are colon or colorectal cancer cells, lung or breast cancer cells, and wherein said mammalian cancer cells are exposed to chemotherapy or radiation therapy, and the claims of 09/396,746 and 10/207,295 are drawn to methods of inducing apoptosis in mammalian cells expressing the Apo-2 receptor of SEQ ID NO: 1, which may be cancer cells. It would be *prima facie* obvious to one of ordinary skill in the art to practice the methods with any cells expressing Apo-2 and with the various types of antibodies or antibody derivatives claimed. Claims 76-78 and 90-92 of the instant application are not included in the provisional rejection because they are drawn to methods using the specific single chain antibodies of 16E2, 20E6, 24C4, and claims 6-9 of 09/396,746 are drawn to specific monoclonal antibodies produced by hybridomas.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent 6,072,047 is cited in IDS paper No. 4 and teaches an Apo-2 polypeptide called TRAIL-R of SEQ ID NO: 2. This patent receives benefit of priority to 08/829,536, filed March 28, 1997, for the full-length receptor polypeptide, which is identical to SEQ ID NO: 1 of the instant application with the exception that TRAIL-R has a 39 amino acid insert beginning after position 182 of SEQ ID NO: 2 of the patent. However, the concept of agonistic antibodies does not appear until priority application 08/869,852, filed June 4, 1997, and the artisan of

ordinary skill would have no motivation to practice the claimed method with an agonistic antibody based on the disclosure of the '536 application. This patent is, therefore, disqualified as prior art. As an aside, it is noted that the concept of antagonistic antibodies is taught in 08/869,852.

US Patent 6,342,369 shares common inventors with the instant application. The claimed subject matter is different from that being claimed in the instant application. This patent is not available as prior art, the earliest possible effective filing date being later than the effective filing date of the instant application.

US Patent 6,313,269 is made of record. This patent is not available as prior art because it does not receive priority before August 22, 1997, for while the full sequence of Apo-2 is disclosed in 08/853,684, filed May 9, 1997, there is no contemplation of agonistic antibodies and the artisan of ordinary skill would have no motivation to practice the claimed method based on the disclosure of the '684 application with an agonistic antibody. Additionally, its provisional application 60/041,230 (Mar. 14, 1997) only discloses amino acids 109 to 411 of SEQ ID NO: 1 of the instant application, which is not sufficient basis for anticipation or obviousness of the claimed invention. Additionally, it is noted that amino acids 32 and 106 are different between SEQ ID NO:2 of the patent 6,313,269 and SEQ ID NO: 1 the instant application.

Conclusion

12.1 Claims 76-78 and 90-92 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12.2 Claims 59-62 and 65-75, 79-89 and 93-97 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner

Notice to Comply	Application N .	Applicant(s)	
	10/052,798	Adams et al.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: sequences are present in Fig. 2B that are not present in the sequence listing.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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